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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,006	07/15/2003	Beverly L. Davidson	17023.013US2	9111
53137 7590 05/30/2007 VIKSNINS HARRIS & PADYS PLLP P.O. BOX 111098 ST. PAUL, MN 55111-1098			EXAMINER BLUMEL, BENJAMIN P	
			ART UNIT 1648	PAPER NUMBER
			MAIL DATE 05/30/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/621,006	Applicant(s) DAVIDSON ET AL.	
	Examiner Benjamin P. Blumel	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on March 2, 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-9 and 11-32 is/are pending in the application.
- 4a) Of the above claim(s) 22 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 24-31 is/are allowed.
- 6) ☒ Claim(s) 1,14-21 and 24-32 is/are rejected.
- 7) ☒ Claim(s) 3-9 and 11-13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>March 2, 2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments and/or amendments.

Claim Amendments

New claims 25-32 are acknowledged; therefore, claims 1, 3-9 and 11-32 will be examined.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on March 2, 2007 was filed after the mailing date of the Non-Final Rejection on October 26, 2006. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

Claims 3-9, 12 and 13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 presently depends on the cancelled claim 10.

Response to Arguments

Applicant's arguments see page 9, lines 16-22, filed March 2, 2007, with respect to the rejection(s) of claim(s) 1, 2 and 14-21 under 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of newly found prior art references, see rejection below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claimed invention as recited in claim 24 states "wherein the polynucleotide encoding a chimeric Ad fiber polypeptide ...encodes SEQ ID NO:12, encodes nucleotides 1-564 of SEQ ID NO:12, encodes nucleotides 1-135 of SEQ ID NO:12, encodes nucleotides 136-564 of SEQ ID NO:12". It is unclear how a polynucleotide can further encode the nucleotides of SEQ ID NO:12. For example, perhaps an amendment reciting "wherein the polynucleotide of SEQ ID NO:12, and nucleotides 1-564, 1-135, or 136-564 of SEQ ID NO:12 encode the chimeric Ad fiber polypeptide of SEQ ID NO:1, amino acids 46-188, 189-371 or 1-45 of SEQ ID NO:1, respectively" would clarify. Additionally, perhaps placing these nucleic acid and/or amino acid sequences in separate dependent claims would also clarify. In addition, it is unclear how the recitation of "a chimeric adenovirus (Ad) fiber polypeptide comprising a tail region, a shaft region and a knob region" can be encoded by amino acids 46-188, 189-371 or 1-45 since these

Art Unit: 1648

amino acid sequences represent either the knob, tail or shaft but not all three combined.

Conversely, an amended recitation stating "...a chimeric Ad fiber polypeptide encodes SEQ ID NO:1..." (see line 4 and 5 of claim 24) might address this issue. However, if applicants wish to retain the limitations of the specific amino acid ranges, perhaps amending claim 24 at line 3 to recite "...a chimeric adenovirus (Ad) fiber polypeptide comprising at least one of the following: a tail region, a shaft region or ~~and~~ a knob region" would clarify the claimed invention. It is also unclear if the claimed invention of claim 24 requires all of the sequences in complete form or in fragments since it appears that these are a Markush group and should be in the alternative.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 14-21 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi et al. (US 6,998,263), Zabner et al. (Journal of Virology, 1999), Chillon et al. (Journal of Virology, 1995) and Davidoff et al. (Journal of Surgical Research, 1999).

Kovesdi et al. teach the development of adenoviruses with altered cellular tropisms by producing various chimeric coat proteins (i.e. fiber, penton) by introducing nonnative viral proteins (i.e. fiber proteins with different subgroup regions combined). Kovesdi et al. teach that by altering these proteins, one in the art may generate vectors deficient in CAR binding and yet able to target and infect cells. The alteration of these proteins provides for distinct immunogenic viruses that should avoid neutralization by a humoral immune response and to provide an adenovirus selective for a potential host cell in gene therapy. The adenoviruses utilized can be from subgroups A-F, preferably, such as Ad5 or Ad30. In addition, Kovesdi et al. teach the use of these adenovirus vectors to express therapeutic agents/genes (i.e. a growth factor, a cytokine, an apoptotic agent, or an angiogenic factor, etc). However, though Kovesdi et al. teach the importance of generating chimeric adenovirus fiber proteins to tailor the cell specific infectivity as part of gene therapy, they do not specifically state an expression vector with an adenovirus fiber protein with an Ad5 tail and Ad30 shaft and knob or the specific target cells (HUVEC, or tumor related cells).

Zabner et al. teaches enhanced genetic transfer with an adenovirus vector comprising a chimeric fiber polypeptide. Several wild-type adenoviruses from groups A-F, were compared in the ability to infect human epithelial cells. Wild-type Ad2 (group C) was 43 times less efficient than Ad17 (group D), also a wild type. Therefore, to examine if the fiber protein of Ad17 might enhance the infection rate of Ad2 Zabner et al. compared the ability of Ad2/ β gal and Ad2/Ad17/ β gal, a chimeric, to infect epithelial cells. The chimeric adenovirus transferred the β gal gene more efficiently resulting in a rate of 15-95 times more β gal expression as compared to Ad2/ β gal.

Art Unit: 1648

Chillon et al. teaches the different infection efficiencies of the multiple Adenovirus groups. Chillon et al. compared the ability of serotypes from groups A-F at infecting human umbilical vein endothelial cells (HUVEC) and central nervous system (CNS) cells. The following serotypes were used in the comparison: Ad31 of group A, Ad3, 7, and 14 of group B, Ad2 of group C, Ad9, 17, 19, 26 and 30 of group D, Ad4 of group E and Ad41 of group F. Following a 48-hour incubation period, post-infection, it was determined the adenovirus serotypes representing groups B and D had the highest rate of infection of HUVEC (20-60% and 20-90% respectively) and groups D and F infected CNS cells most efficiently (20-60% and 40% respectively). Of the least efficient serotypes to infect the target cells, Ad2 and 31 infected 5% of the CNS cells but did not infect HUVEC. The serotype able to infect the highest percentage of both target cell types was Ad30, 60% for CNS cells and 90% for HUVEC. Chillon et al. further experimented with a chimeric fiber Adenovirus, testing the ability of ligating a portion of Ad17 fiber replacing most of the Ad2 fiber. A comparison was made between a chimeric Ad2 β gal2(17f) and Ad2 β gal2 incubating with HUVEC and CNS cells. The later proved to be 21-fold and 7-fold less efficient at transferring the β gal gene.

Davidoff et al. teaches a method of improving an anti-tumor vaccine by altering the adenovirus vector of Ad5 with a chimeric fiber protein, which has the knob region of Ad3 and the shaft/tail regions of Ad5. This recombinant vector proved to have an increased transduction of a heterologous gene among the cancerous cell cultures when compared to the un-altered Ad5 vector. Therefore, Davidoff et al. concludes that utilizing adenoviruses chimeric fiber proteins can result in achieving optimum gene delivery *in situ* with a smaller viral dosage.

It would have been obvious to one of ordinary skill in the art to modify the method taught by Kovesdi et al. in order to transduce a CAR lacking cell with an adenovirus vector that had chimeric fiber polypeptide with a region from Ad30, thereby enhancing the administration of a therapeutic agent to a targeted cell/tissue. One would have been motivated to do so, given the suggestion by Kovesdi et al. that the modifying the coat proteins (fiber, penton) as discussed above, can improve the delivery of a therapeutic gene expressed by an adenoviral vector to a specific host cell. There would have been a reasonable expectation of success, given the knowledge that forming a chimeric fiber comprising the knob, shaft and part of the tail from Ad17 and the remainder of the tail from Ad2 provided a more efficient transfer of genes to target cells as compared with Ad2-wild type, as taught by Zabner et al., also given the knowledge that serotypes from groups B and D, particularly Ad30 and 17, offer a more efficient infectivity of HUVEC and CNS cells (cells lacking CAR), as taught by Chillon et al., and also given the knowledge that a recombinant adenovirus therapeutic vector with a chimeric fiber protein improved gene delivery to a series of tumor cell lines. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Summary

No claims are allowed.

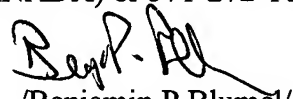
Conclusion

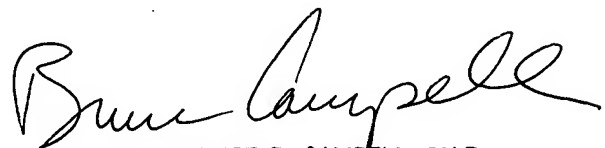
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin P. Blumel whose telephone number is 571-272-4960. The examiner can normally be reached on M-F, 8-4:30.

Art Unit: 1648

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campbell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


/Benjamin P Blumel/
Examiner
Art Unit 1648


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